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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/560,455

12/14/2005

Silvia Gluck

13111-00027-US

3072

23416

7590

04/30/2010

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EXAMINER

MARX, IRENE

ART UNIT

PAPER NUMBER

1651

MAIL DATE

DELIVERY MODE

04/30/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/560,455	Applicant(s) GLUCK ET AL.	
	Examiner Irene Marx	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 January 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5,6,18-21 and 28-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5,18-21,28,29 and 31-34 is/are rejected.
- 7) ☐ Claim(s) 6 and 30 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/5/10</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The amendment filed 1/19/10 is acknowledged.

Claims 1, 5-6, 18-21 and 28-34 are being considered on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5-6, 18-21 and 28-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stetter *et al.*, taken with DSMZ Catalogue, Mori *et al.* and Seufer-Wasserthal *et al.* (U.S. Patent No. 5,534,436).

The claims are directed to a process of isomerization of an α -hydroxycarboxylic acid with an enzyme in a reaction medium, wherein the enzyme is contained in an extract or present in intact cells of a *Lactobacillus* or *Lactococcus* and optionally isolating the mixture obtained and chemical or enzymatically treating it further.

Stetter *et al.* discloses a process of isomerization an α -hydroxycarboxylic acid with *Lactobacillus* strains *L. paracasei* subsp. *paracasei* DSM 20207 (DSM 15755), *L. delbrueckii* ATCC 9649 which is identical to DSM 20074 (DSM 15754) and *L. sakei* ATCC 15521, which is identical to DSM 20017 (DSM 15753) in the process (See, e.g., page 225-226 and Figure, page 237), as adequately demonstrated by DSMZ Catalogue, see, e.g., item 906, which is the Stetter *et al.* reference and applicant's proffer. It is clear that at least these three *Lactobacillus* strains contain the enzymatic activity required for the claimed process and are capable thereof.

The reference differs from the claimed invention in the substrates submitted to the isomerization reaction. However, one of ordinary skill in the art would have recognized at the time the claimed invention was made that the substrate specificity of the enzyme extracts or

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microbial cells provided by Stetter *et al.* is not limited to the disclosed substrate and would have been motivated to test further substrates with a reasonable expectation of success by using microbial enzymes from *Lactobacillus* including the enzymes produced by or present in the extracts or cells of the strains recited, including *L. paracasei* subsp. *paracasei* DSM 20207 (DSM 15755), *L. sakei* ATCC 15521, DSM 20017 (DSM 15753) and *L. delbrueckii* ATCC 9649, DSM 20074 (DSM 15754) which are clearly inherently "capable" of isomerizing at least one compound from the list in claim 1, since they are strains indicated as particularly suitable in the process in the as filed specification. In addition, Mori *et al.* suggest further substrates in their teachings that products such as D-mandelic acid are useful as raw materials or intermediates in the preparation of pharmaceuticals such as antibiotics and ephedrin. See, e.g., page 2, lines 2-4.

The reference differs from the invention as claimed in that further enzymatic or chemical modifications are not recited. However, Mori *et al.* adequately show that it was well known in the art at the time the claimed invention was made to modify compounds obtained in isomerization or resolution reactions by converting a racemic compound into an optically active isomer. See, e.g., Examples. In addition, Seufer-Wasserthal *et al.* disclose the chemical or enzymatic enantioselective subsequent reaction that comprises esterification. See, e.g., col. 2, bridging paragraph between col. 2 and 3.

It is noted that invention of new claims 28-29 and 31-34 does not require a particular screening method, but rather only indicates "screening and obtaining" *Lactobacillus* or *Lactococcus* having a certain ability. No specific process steps are recited. In this regard, it must be remembered that of the strains screened and selected by the Stetter reference include at least the strains *L. paracasei* subsp. *paracasei* DSM 20207 (DSM 15755), *L. delbrueckii* ATCC 9649 which is identical to DSM 20074 (DSM 15754) and *L. sakei* ATCC 15521, which is identical to DSM 20017 (DSM 15753) are the identical strains as screened and selected by applicant. These strains are inherently capable of the claimed racemization process as claimed.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of Stetter *et al.* by using a variety of *Lactobacillus* strains and substrates such as mandelic acid, as suggested by Mori *et al.* and submitting the resultant product to further reactions such as esterification as suggested by the teachings of Mori *et al.* and Seufer-Wasserthal *et al.* for the expected benefit of obtaining

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pharmaceutically valuable optically active compounds that are important *per se* or which are useful intermediates to produce further optically active pharmaceuticals.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

The crux of Applicant(s) argument is that "not every *Lactobacillus* strain" possesses a positive racemization activity as required by the claims, even though the claims as written encompass any and all *Lactobacillus* or diverse members of four species of *Lactobacillus* and any *Lactococcus* whatsoever. Applicant goes on to state that Example 2 and Table 6 at pages 33-34 of the specification demonstrate that "only a few" strains of *Lactobacillus* showed a positive racemization activity with the substrates used in the exemplified screening procedure. Yet, as noted, the claims are directed to any *Lactobacillus* or to diverse members of four species of *Lactobacillus* and any *Lactococcus*.

Applicant also argues that they are not aware of any prior art reference teaching or suggesting a suitable procedure for screening and obtaining the *Lactobacillus* strains with the required racemization activity. It is not apparent that the claimed method is particularly effective at identifying further *Lactobacillus* or members of certain species of *Lactobacillus* or members of *Lactococcus*, since no further strains are shown other than those specific strains of Example 2 and Table 6 at pages 33-34 of the specification

As to the screening method touted, it is noted that the claimed invention does not require a particular screening method, but rather only indicates "screening and obtaining" *Lactobacillus* or *Lactococcus* having a certain ability. No specific process steps are recited. In this regard, it must be remembered that of the strains selected by the present method at least the strains *L. paracasei* subsp. *paracasei* DSM 20207 (DSM 15755), *L. delbrueckii* ATCC 9649 which is identical to DSM 20074 (DSM 15754) and *L. sakei* ATCC 15521, which is identical to DSM 20017 (DSM 15753) are disclosed by Stetter. These strains are inherently capable of the claimed racemization process as claimed.

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In addition, as noted, the results of the tables demonstrate that no further strains other than the specific strains recited in claims 6 and 30 are obtained or identified by the screening method as being capable of the required racemization. Furthermore, any microbiological process requires "screening" prior to applying a microorganism to a process to determine its suitability.

Accordingly, applicant's arguments are persuasive only with respect to the specific strains shown to be effective in achieving the claimed process. The results shown for a few *Lactobacillus* strains suitable for the claimed invention are not commensurate in scope with the claims directed to any *Lactobacillus* or any *Lactococcus* or any *L. oris* or any *L. delbrueckii* or any *L. sakei* or any *L. paracasei*. The arguments regarding the surprising discovery of racemization activity for a panel of structurally different substrates only pertains to the specific strains shown. The unexpected and significant results obtained are limited to the demonstrated strains.

It is noted that obviousness does not require absolute predictability, however, at least some degree of predictability is required. In the present case, even though Stetter does not disclose a bioconversion specific of the range of substrates of the present process by using extracts or cells of *Lactobacillus* or *Lactococcus*, it is submitted that the three disclosed strains of *Lactobacillus* disclosed by the reference are clearly "capable" of the bioconversion of further substrates as listed, even if this capacity is not explicitly disclosed in the reference. In addition, it is of interest to note that there is not a single *Lactococcus* strain identified and shown in the present record to have the required bioconversion capability.

Moreover, as noted, it is not apparent from the as-filed specification that any and all *Lactobacillus* or any and all *Lactococcus* strains or even all strains within the broad species recited in claims 5 and 29 have the touted capabilities.

The scope of the showing must be commensurate with the scope of claims to consider evidence probative of unexpected results, for example. In re Dill, 202 USPQ 805 (CCPA, 1979), In re Lindner 173 USPQ 356 (CCPA 1972), In re Hyson, 172 USPQ 399 (CCPA 1972), In re Boesch, 205 USPQ 215, (CCPA 1980), In re Grasselli, 218 USPQ 769 (Fed. Cir. 1983), In re Clemens, 206 USPQ 289 (CCPA 1980). It should be clear that the probative value of the data is not commensurate in scope with the degree of protection sought by the claim.

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Therefore the rejection is deemed proper and it is adhered to.

Claims 6 and 30 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten as suggested in the proposed amendment sent to applicant by facsimile on April 13, 2010.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Irene Marx whose telephone number is (571) 272-0919. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 .

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Irene Marx/
Primary Examiner
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